REMARKS

Claim 1 has been amended to describe the inventive subject matter more clearly. Upon entry of the above amendments, claims 1-4, 6-11, and 23-38 are pending in the application.

The amendments do not introduce new matter within the meaning of 35 U.S.C. §132. Basis for the claim amendments is found on page 15, line 17 to page 18, line 24; page 44, line 1 to page 51, line 30; in claim 1 as originally filed; and elsewhere throughout the specification and claims. Accordingly, entry of the amendments is respectfully requested.

INTERVIEW SUMMARY

Applicants take this opportunity to thank Examiners Owens and Geist for their courtesy and time in conducting an interview with Applicants' counsel on August 3, 2001. While agreement was not reached during the interview, the opportunity to discuss the outstanding rejections and to narrow the issues for appeal was appreciated.

1. Rejection of Claims 1-4, 6-11, and 23-38 under Judicially Created Doctrine of Obviousness-type Double Patenting

A. Rejection over U.S. Patent No. 6,140,357. The Office Action rejects claims 1-4, 6-11, and 23-38 as being unpatentable

over claims 1-11 of U.S. Patent No. 6,140,357 (the '357 patent), under the judicially created doctrine of obviousness-type double patenting. As the basis for this rejection, the Office Action states that although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to a method of effecting or treating neuronal activity in an animal with the same or analogous compounds. The Examiner concludes that the treatment of memory disorders and nerve-related vision disorders is thus *per se* obvious over the claims of the '357 patent.

The Office Action further states that the claims of the present application differ from the '357 patent "...only through the claim language of treating vision disorders." Contrary to the Office Action, the **compounds** used in the methods of the '357 patent are distinct from the compounds of the present claims. In particular, the substituent attached to the 2-position of the '357 patent compounds is required to be an ester or amide, which is in turn required to be further substituted. In contrast, in the compounds of the present invention, the substituent attached to the 2-position is (1) not permitted to be either an ester or amide and (2) is not permitted to be further substituted.

An obvious-type double patenting rejection should make clear: (A) the differences between the inventions defined by the

conflicting claims, and (B) the reasons why a person of ordinary skill in the art would conclude that the claim in issue is an obvious variation of the claim in the patent or second application (MPEP §804, paragraph II.B.1). Although the *uses* claimed in the '357 patent and the present application are also patentably distinct for the reasons discussed below, in any event the compounds used in the respective methods are distinct. The Office Action does not recognize the difference in the compounds. Further, the Office Action does not attempt to give reasons why one of ordinary skill in the art would conclude that the claims of the present invention are an obvious variation of the claims of the '357 patent, given that both the compounds used and the methods of use are different. Thus, the Office Action fails to establish a *prima facie* case of obviousness-type double patenting.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw this rejection as to the '357 patent.

B. Provisional rejection over copending application no. 09/453,571. The Office Action rejects claims 1-4, 6-11, and 23-38 as being unpatentable over claims 16-23 of U.S. Patent Application No. 09/453,571 (the '571 application), under the judicially created doctrine of obviousness-type double patenting. As the basis for this rejection, the Office Action states that although the conflicting claims are not identical, they are not patentably

distinct from each other because they are drawn to a method of effecting or treating neuronal activity in an animal with the same or analogous N-heterocyclic compounds. The Examiner concludes that the treatment of memory disorders and nerve-related vision disorders is thus *per se* obvious over the claims of the '571 application.

Any obvious-type double patenting rejection should make clear: (A) the differences between the inventions defined by the conflicting claims, and (B) the reasons why a person of ordinary skill in the art would conclude that the claim in issue is an obvious variation of the claim in the patent or second application (MPEP §804, paragraph II.B.1). Further, the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966), for determining obviousness under 35 U.S.C. §103 should be employed when making an obviousness-type double patenting rejection (*In re Braat*, 937 F.2d 589, 19 U.S.P.Q.2d 1289, 1292 (Fed. Cir. 1991); MPEP § 804, paragraph II.B.1). The Office Action fails to discuss the differences between the purportedly conflicting claims and the *reasons* for concluding that the present claims are obvious variations of claims 16-23 of the '571 application; the Examiner merely concludes, without stating any reasons, that methods for "treating nerve-related vision disorders" and for "treating memory impairment" are methods for "effecting or treating neuronal

activity."

Without waiving the aforementioned deficiencies, Applicants respectfully traverse the double patenting rejection on the ground that the instantly claimed invention is patentable over the invention claimed in the '571 application.

A. Treating Vision Disorders Is Patentably Distinct from Treating a Neurological Disorder

An obviousness-type double patenting rejection is improper where the application claims are patentably distinct from the prior patent claims. The '571 application claims methods for "treating a neurological disorder" by administering a compound of the invention to "stimulate the growth of peripheral nerves or to promote neuronal regeneration" (see claim 16). Contrary to the Office Action, the '571 application does not claim methods for treating all "conditions which have a neurological basis".

Like *In re Kaplan*, 229 U.S.P.Q. 678 (Fed.Cir. 1986), the instant obviousness-type double patenting rejection involves dominating claims ("treating a neurological disorder" by administering a compound of the invention to "stimulate the growth of peripheral nerves or to promote neuronal regeneration" in the '571 application) and later-filed improvement claims (the present claims to "treating a nerve-related vision disorder"). As Kaplan makes clear, *prima facie* evidence in support of an obviousness-type double patenting rejection must include "some clear evidence to

establish why the variation would have been obvious which can properly qualify as 'prior art'," including prior art evidence of the level of skill in the art if that is what the rejection is based upon (Id. at 683). However, the specification of the dominating patent **cannot** be used as prior art (Id. at 682, citing with approval *In re Vogel*, 164 U.S.P.Q. 619 (CCPA 1970).)

Like *In re Kaplan*, the only references cited in the Office Action to show that the presently claimed invention is an obvious variant of the invention claimed in the '571 application are the '571 application itself and the Applicants' specification. Lacking any other reference to support the rejection, it is clear that the Examiner has engaged in hindsight, using Applicants' specification to show obviousness. Thus, the Office Action fails to establish a *prima facie* case of obviousness-type double patenting in relation to vision disorders.

B. Treating Memory Disorders Is Patentably Distinct from Effecting a Neuronal Activity

The '571 application claims methods for "treating a neurological disorder" by administering a compound of the invention to "stimulate the growth of peripheral nerves or to promote neuronal regeneration" (claim 16). Claims 17 and 18 of the cited application further claim treatment of the following specific neurological disorders: peripheral neuropathy caused by physical injury or disease state, physical damage to the brain, physical

damage to the spinal cord, stroke associated with brain damage, and neurological disorders relating to neurodegeneration, specifically Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. Contrary to the Office Action, nowhere does the '571 application claim a method for treating a memory disorder.

The present application claims methods for "treating memory impairment". Contrary to the Office Action, the present application does not claim "treating the neurological basis or etiology of ... memory impairment." While the Examiner contends that based on the '571 application claims to "treating or effecting neuronal activity ... one of skill in the art would certainly have a reasonable expectation of success in the use of these compounds to treat conditions which have a neurological basis...", the Examiner does not provide the required factual or technical grounds establishing such relationship; the mere possibility or probability that a certain thing may result from a given set of circumstances, here a mere "reasonable expectation of success," is **not** sufficient. As discussed above, "some clear evidence to establish why the variation would have been obvious which can properly qualify as 'prior art'," must be shown; the Examiner's bare conclusion that there is a "reasonable expectation of success" is not a sufficient showing of prior art. Lacking any showing in the art of specific motivation to use the compounds claimed in the '571 application in

the methods of the present invention, the Office Action does not establish a *prima facie* case of obviousness.

Contrary to the Office Action, the art teaches that one cannot predict that compounds useful for treating diverse neurological conditions such as brain trauma, stroke, and the diseases of Alzheimer and Parkinson, would be effective for treating memory impairment. For example, the antidepressant Imipramine is useful in the treatment of Alzheimer's disease, but is not effective in treating the associated memory impairment. Teri et al., *J. Gerontol.*, 46 (1991) 372-377; copy enclosed. Similarly, Levodopa is useful in the treatment of Parkinson's disease, but does not affect the associated memory dysfunction. Owen et al., *Neuropsychologia*, 35 (1997) 519-532; copy enclosed.

At best, the '571 application might make it obvious to try neurotrophic compounds for treating memory disorders. However, lacking any direction for selecting successful compounds or indication of critical parameters, this is insufficient to support a determination of obviousness. Thus, the Office Action fails to establish a *prima facie* case of obviousness-type double patenting in relation to memory disorders as well.

In the absence of any teaching or suggestion in the '571 application that carboxylic acids and isosteres of N-heterocyclic compounds used for treating neurological disorders by administering

a compound to "stimulate the growth of peripheral nerves or to promote neuronal regeneration" would also be useful for treating nerve-related vision disorders or for treating memory impairment, the claims of the present application clearly are unobvious over the claims of the '571 application.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw this rejection.

2. Rejection of Claims 1-4, 6-11, and 23-38 under 35 U.S.C. §103(a)

The Office Action rejects claims 1-4, 6-11, and 23-38 as being unpatentable over U.S. Patent Number 6,140,357 ("the '357 patent"). As the basis for this rejection, the Office Action states that the '357 patent teaches that the use of identical or analogous compounds "for the treatment of memory impairment." While admitting that the '357 patent does not teach treating vision disorders, the Examiner nevertheless argues that treating "neurological activity" in the '357 patent makes it *prima facie* obvious to treat nerve-related vision disorders.

The Office Action states that the '357 patent teaches methods purportedly related to those of the present invention using "...the analogous compounds set forth in the instant claims." Contrary to the Office Action, the **compounds** used in the methods of the '357 patent are distinct from the compounds of the present claims. In

particular, the substituent attached to the 2-position of the '357 patent compounds is required to be an ester or amide, which is in turn required to be further substituted. In contrast, in the compounds of the present invention, the substituent attached to the 2-position is (1) not permitted to be either an ester or amide and (2) is not permitted to be further substituted.

Although the *uses* claimed in the '357 patent and the present application are also patentably distinct for the reasons discussed below, in any event the compounds used in the respective methods are distinct. The Office Action does not recognize the difference in the compounds. Further, the Office Action does not attempt to give reasons why it would be obvious to one of ordinary skill in the art would use the reference compounds in the methods of the present invention, given that both the compounds used and the methods of use are different. Thus, the Office Action fails to establish a *prima facie* case of obviousness.

Applicants respectfully further traverse this rejection. The Examiner relies on his own generalizations to mischaracterize both the '357 patent and the present inventive subject matter. The '357 patent absolutely does **not** mention either memory impairment or vision disorders of any sort.

Applicants respectfully traverse the above rejection. The '357 patent does not teach or suggest Applicants' inventive subject

matter as a whole, as recited in the amended claims. Further, the art teaches the ordinarily skilled artisan away from the subject matter as defined in the claims.

The U.S. Supreme Court in *Graham v. John Deere Co.*, 148 U.S.P.Q. 459 (1966) held that non-obviousness was determined under §103 by (1) determining the scope and content of the prior art; (2) ascertaining the differences between the prior art and the claims at issue; (3) resolving the level of ordinary skill in the art; and, (4) inquiring as to any objective evidence of nonobviousness. In applying the *Graham* test, all of the facts must be considered; it is not acceptable within the framework of §103 to pick and chose from certain facts that support a position. Rather, all of the facts of the prior art and the instant invention must be taken into account.

A. The present inventive subject matter

Applicant's claims as presently amended are directed to a method for treating specified nerve-related vision disorders or treating memory impairment in an animal, which comprises administering to said animal an effective amount of a carboxylic acid, or isostere thereof, of N-heterocyclic compounds.

B. The prior art

As discussed above regarding the rejection under the judicially created doctrine of obviousness-type double patenting,

the '357 patent discloses a method for "treating a neurological disorder" by administering a compound of the invention to "stimulate the growth of peripheral nerves or to promote neuronal regeneration," wherein the neuronal activity is selected from the group consisting of "stimulation of damaged neurons, promotion of neuronal regeneration, and treatment of neurological disorder". The '357 patent recites conditions such as peripheral neuropathy, physical damage to the brain, physical damage to the spinal cord, stroke associated with brain damage, Alzheimer's Disease, Parkinson's Disease, and amyotrophic lateral sclerosis as examples of such neurological disorders.

C. The differences between the claimed subject matter and the prior art

To establish a *prima facie* case, the PTO must satisfy three requirements. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference. *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). Second the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). Third, the prior art

reference must teach or suggest all the limitations of the claims. *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970).

In the present case, a legally sufficient *prima facie* case of obviousness must include a showing of the reasons why it would be obvious to use one or more reference compound(s) for the claimed utilities of the present invention. Here, the cited reference does not teach or suggest the use of any compound claimed in the present application for treating any form of memory impairment or for treating any type of vision disorder.

Treating Vision Disorders. For the reasons discussed above, whether denominated obviousness-type double patenting or obviousness under §103(a), improvement claims are not obvious over dominating patents. As *In re Kaplan* and *In re Fine* make clear, *prima facie* evidence in support of an obviousness-based rejection must include some clear prior art evidence to establish obviousness. Lacking any other cited reference(s), and in the absence of any teaching or suggestion in the '357 patent that the carboxylic acids and isosteres of N-heterocyclic compounds used for treating neurological disorders would also be useful for treating vision disorders, the claims of the present application cannot be obvious over the '357 patent.

Treating Memory Disorders. While some of the conditions disclosed in the '357 patent may present with memory impairment as one of their many symptoms, memory impairment can also occur in the absence of a disease or trauma, for example, as a consequence of age alone (see specification, pg. 21). Even where memory impairment manifests as a symptom of a neurological disorder, the etiology of the underlying disorder is often unknown. Without knowing how the claimed methods in either the '357 patent or the present application operate, or how the compounds used in the claimed methods elicit the desired effect, one cannot predict that compounds useful for treating a neurological disorder would be effective for treating memory impairment. For example, as discussed above, the antidepressant Imipramine is useful in the treatment of Alzheimer's disease, but is not effective in treating the associated memory impairment. Teri et al., *J. Gerontol.*, 46 (1991) 372-377; copy enclosed. Similarly, Levodopa is useful in the treatment of Parkinson's disease, but does not affect the associated memory dysfunction. Owen et al., *Neuropsychologia*, 35 (1997) 519-532; copy enclosed. Thus, in the absence of any teaching or suggestion in the '357 patent that the carboxylic acids and isosteres of N-heterocyclic compounds used for treating neurological disorders would also be useful for treating memory impairment, the claims of the present application cannot be obvious

over the '357 patent.

The discovery of a new use for an old compound based on unknown properties of the structure is patentable to the discoverer as a process of using. *In re Hack*, 245 F.2d 246, 248, 114 USPQ 161, 163 (CCPA 1957). In order to expedite prosecution and place the application in condition for allowance or appeal, Applicants have amended claim 1 to entirely exclude Alzheimer's disease and Parkinson's disease at this time (despite the fact that the art at the time the application was filed taught *only* that treating some non-memory aspects of multi-faceted diseases such as Alzheimer's and Parkinson's diseases does not treat associated memory impairment). These amendments are made without prejudice or disclaimer of any subject matter therein, and Applicants reserve the right to pursue any or all subject matter removed from this application in the restricted, canceled, or amended claims in a continuing application.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

3. Provisional Rejection of Claims 1-4, 6-11, and 23-38 under 35 U.S.C. §103(a)

The Office Action states that it provisionally rejects claims 1-4, 6-11, and 23-38 as being unpatentable over U.S. Patent **Application** No. 09/453,571. For the reasons discussed above in

response to the obviousness-type double patenting rejection, the present application is non-obvious over the '571 application.

However, a more fundamental problem exists with regard to this purported rejection--it is non-statutory. Section 103(a) permits the use of various categories of prior art described in section 102 as the basis for obviousness rejections. A pending U.S. Patent **Application** which has not published is not a valid reference under any subsection of §102.

Apparently recognizing that the '571 application is not a valid reference, the Examiner has attempted to create a new type of rejection. However creative, the Examiner has cited no statute or case law supporting the existence of a "provisional obviousness" rejection. The Office Action cites only §103(a), which does not permit a "provisional" rejection.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

CONCLUSION

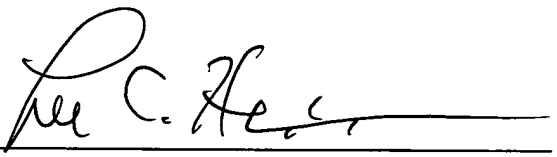
Based upon the foregoing amendments and remarks, the presently claimed subject matter is definite, enabled, and patentably distinguishable over the art of record. The Examiner is therefore respectfully requested to reconsider and withdraw the rejections of claims 1-4, 6-11, and 23-38 and allow pending claims 1-4, 6-11, and

23-38 presented herein for reconsideration. Favorable action with an early allowance of the pending claims is earnestly solicited.

The Examiner is invited to telephone the undersigned attorney if he has any questions or comments.

Respectfully submitted,

NATH & ASSOCIATES PLLC

Dated: September 13, 2001 By: 

Gary M. Nath
Reg. No. 26,965
Todd L. Juneau
Reg. No. 40,669
Lee C. Heiman
Reg. No. 41,827
Customer No. 20529

NATH & ASSOCIATES PLLC
1030 Fifteenth Street, NW
Sixth Floor
Washington, D.C. 20005
Telephone: (202) 775-8383
Facsimile: (202) 775-8396
GMN:TLJ:LCH RFR2.wpd

Appendix 1

Amendments to pending claims: mark-up copy (37 C.F.R. §1.121(c) (ii)).

Please amend claim 1 as follows:

1. (Four times amended) A method for treating a nerve-related vision disorder or treating memory impairment in a mammal in need thereof, which comprises administering to said mammal an effective amount of a heterocyclic compound which has a carboxylic acid substituent, or isostere thereof, attached to the 2-carbon of the heterocyclic ring and which additionally has a diketo or thioketo nitrogen-linked substituent attached to the heterocyclic ring [an N-heterocyclic ring compound containing a carboxylic acid or carboxylic acid isostere moiety thereof attached to the 2-carbon of the N-heterocyclic ring],

wherein the nerve-related vision disorder is selected from the group consisting of the following:

visual impairments;

orbital disorders;

disorders of the lacrimal apparatus;

disorders of the eyelids;

disorders of the conjunctiva;

disorders of the cornea;

cataract;

disorders of the uveal tract;

disorders of the retina;

disorders of the optic nerve or visual pathways;

free radical induced eye disorders and diseases;

immunologically-mediated eye disorders and diseases;

nerve-related physical injury affecting vision; and

nerve-related symptoms and complications of eye disease, nerve-related symptoms and complications of eye disorders, and nerve-related symptoms and complications of physical injury affecting vision;

provided that said memory impairment is not a neurological disorder relating to neurodegeneration selected from the group consisting of Alzheimer's Disease and Parkinson's Disease.

Appendix 2

Clean copy of all amended claims (claim 1) (37 C.F.R. §1.121(c)(i)).

1. (Four times amended) A method for treating a nerve-related vision disorder or treating memory impairment in a mammal in need thereof, which comprises administering to said mammal an effective amount of a heterocyclic compound which has a carboxylic acid substituent, or isostere thereof, attached to the 2-carbon of the heterocyclic ring and which additionally has a diketo or thioketo nitrogen-linked substituent attached to the heterocyclic ring,

wherein the nerve-related vision disorder is selected from the group consisting of the following:

visual impairments;

orbital disorders;

disorders of the lacrimal apparatus;

disorders of the eyelids;

disorders of the conjunctiva;

disorders of the cornea;

cataract;

disorders of the uveal tract;

disorders of the retina;

disorders of the optic nerve or visual pathways;

free radical induced eye disorders and diseases;

immunologically-mediated eye disorders and diseases;

nerve-related physical injury affecting vision; and

nerve-related symptoms and complications of eye disease, nerve-related symptoms and complications of eye disorders, and nerve-related symptoms and complications of physical injury affecting vision;

provided that said memory impairment is not a neurological disorder relating to neurodegeneration selected from the group consisting of Alzheimer's Disease and Parkinson's Disease.